DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

g30051

19900 MacArthur Blvd., Ste 300
Irvine, California 92612-2445
Telephone (949) 798-7600

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

December 27, 2001 WL-23-02

Yorman Fishman, President/CEO
2-2-0 Laboratories
2375 Third Street
Riverside, CA 92507

Dear Mr. Fishman:

During an inspection of your manufacturing facility located in Riverside, CA conducted December 5 through December 12, 2001, an FDA investigator documented deviations from the Current Good Manufacturing Practices (cGMPs) for Finished Pharmaceuticals (Title 21, Code of Federal Regulations, (CFR) Part 211). Those deviations cause all drug products manufactured at your facility to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the Act). The violations from 21 CFR Part 211 include:

1. Failure to ensure satisfactory conformance to final specifications through appropriate laboratory determination for both finished drug products and active pharmaceutical ingredients (API) prior to release [211.165(a)]. For example, you failed to conduct finished product testing on at least 6 batches of product since November 7, 2001.

2. Failure to thoroughly review and approve drug product production and control records, investigate unexplained discrepancies, investigate the failure of any batch or any of its components to meet specifications or to extend the investigation to other batches of the same or other drug products that may be affected by the failure [211.192]. For example, several drug products manufactured by your firm containing octyl methoxycinnamate failed specifications and were released; there was no investigation into the cause of the failure of these products to meet specifications.

3. Failure to reject drug products that fail to meet established specifications [211.165(f)]. For example, several drug products manufactured by your firm containing octyl methoxycinnamate failed specifications and were released.

4. Failure to write production and process control procedures designed to assure your drug products have the required identity, strength, quality and purity [211.100(a)]. For example, you have no process validation data for any of your drug products, and you have no

validation that your cleaning and sanitation procedures prevent significant cross contamination from multi-use manufacturing process equipment. Products manufactured at your facility include ingredients such as lead acetate and sulphur.

5. Failure to maintain equipment to prevent malfunctions or contamination that would alter the safety, identity, strength and purity of the drug product [211.67(a)]. For example, you do not clean and sanitize equipment between batches of like products, regardless of production schedule, and cleaning between batches of dissimilar products is inadequate.

6. Failure to write and follow adequate procedures for maintenance and cleaning [211.67(b)]. For example, the procedures detailing the cleaning of equipment does not contain sufficient detail to assure proper cleaning.

7. Failure to ensure that equipment used in the manufacture, processing, packing or holding of drug products is of appropriate design, adequate size, and suitably located for its intended use [211.63]. For example, you have not qualified the performance of manufacturing equipment, including a lack of installation qualification, operation qualification and performance qualification of your autoclave, laminar flow hood, compounding equipment and fillers.

8. Failure to prepare Master Production and Control Records designed to assure batch to batch uniformity that include all required information [211.186]. For example, you have no Master Production Records for any drug products you manufacture.

9. Failure to prepare batch records with complete information relating to the production and control of each batch of drug product [211.188].

10. Failure of the quality control unit to approve or reject all procedures or specifications impacting on the identity, strength, quality, and purity of the drug products [211.22]. For example, our investigators observed unapproved, un-justified changes to the deionized water system.

11. Failure to establish and follow written procedures detailing the receipt, identification, storage, handling, sampling examination and/or testing of labeling materials [211.122].

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility, and encompasses a brief overview of all the violations identified at your facility. It is your responsibility to assure adherence with each requirement of the Good Manufacturing Practice Regulations. Federal agencies are advised of the issuance of all Warning Letters about drugs so that they may take this information into account when considering the award of contracts. Additionally, pending Antibiotic Form 6, New Drug Applications, Abbreviated New Drug Applications or export approval requests may not be approved until the above violations are corrected.

We acknowledge the commitment you made during the inspection to correct the observed deficiencies. However, we note that similar promises were made following previous inspections conducted at your facility, and following the issuance of a Warning Letter to you in June 1998,

and yet the same violations still exist. You should be aware that we consider several of the FDA-483 observations (lack of process validation, lack of written procedures, lack of appropriate investigations, lack of appropriate cleaning and sanitization) to be highly significant. You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. Possible actions include seizure and/or injunction.

In addition, because of the extensive nature of the above cGMP violations, we are asking you to contact this office within five (5) working days of your receipt of this letter to arrange a meeting with us to discuss this matter in person. Please be prepared to discuss the status of all products manufactured by your firm currently in distribution and to provide the District a list of all customers for whom you manufacture drug products at this meeting. You may contact the District Director's Office at (949) 798-7714 to schedule this meeting.

Sincerely

Alonza E. Cruse
District Director

cc: California Department of Health Services, Food & Drug Branch
601 N. 7th Street
Sacramento, California 94234-7320
Attn: Stuart Richardson, Jr., Chief